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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/888,056	06/22/2001	Kenneth Kornman	MSA-023.01	6975
25181	7590	10/17/2003	EXAMINER	
FOLEY HOAG, LLP PATENT GROUP, WORLD TRADE CENTER WEST 155 SEAPORT BLVD BOSTON, MA 02110			CHAKRABARTI, ARUN K	
			ART UNIT	PAPER NUMBER
			1634	

DATE MAILED: 10/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.  
**09/888,056**

Applicant(s)  
**Kornman**

Examiner  
**Arun Chakrabarti**

Art Unit  
**1634**



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on Aug 25, 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-7, 9-23, 26, and 27 is/are pending in the application.
- 4a) Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-7, 9-23, 26, and 27 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some\* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 0903 6) ☒ Other: **Detailed Action**

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## **DETAILED ACTION**

### ***Current Status of the Application***

1. Applicant's amendment filed on August 25, 2003 have been entered. Claims 8, 24, 25 and 28-37 have been cancelled without prejudice towards further prosecution. Claims 1-7, 12, 15-23, and 27 have been amended herein. Claims 1-7, 9-23, and 26-27 are pending in this application.

### ***Double Patenting***

2. Claims 1, 2, 4, 6, 16, 17, 19, 21, and 22 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 48-57 of U.S. Patent No. 6,268,142 B1 (July 31, 2001) in view of Bacus et al. (U.S. Patent 6,031,930) (February 29, 2000).. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 48-57 of U.S. Patent No. 6,268,142 B1 disclose the instant method for identifying a substance that is likely to prevent or diminish a specific biological response in a subject having an inflammatory disease-associated genotype (inherently present in the alleles disclosed in claim 48), the method comprising the steps of:

a) genotyping at least one subject to identify a test subject, wherein the test subject is a subject having an inflammatory disease-associated genotype;

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b) observing in cells obtained from the test subject, or cells propagated therefrom, at least one biomarker (IL-1 protein bioreactivity in this case);

c) contacting the cells obtained from the test subject, or cells propagated therefrom, with a test substance;

d) observing again in the cells obtained from the test subject, or cells propagated therefrom, the at least one biomarker;

wherein a change in the at least one biomarker from an inflammatory disease-associated phenotype to a non-inflammatory disease-associated phenotype identifies a test substance that is likely to prevent or diminish the specific immune response in a subject having the inflammatory disease-associated phenotype.

Claims 48-57 of U.S. Patent No. 6,268,142 B1 also disclose the chromosomal region IL-1RN, and allele 1 of IL-1A(+4845), and biomarker selected from IL-1alpha production.

Claims 48-57 of U.S. Patent No. 6,268,142 B1 do not teach the step of administering an inducer to the test subject prior to or concomitant with observing the biomarker.

Bacus et al teaches the step of administering an inducer to the test subject prior to or concomitant with observing the biomarker (Column 2, lines 17-47, Figure 15, and Column 17, line 56 to Column 18, line 5).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the step of administering an inducer to the test subject prior to or concomitant with observing the biomarker of Bacus et al. in the claims 48-57

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of U.S. Patent No. 6,268,142 B1, since Bacus et al. states "Thus there is a need for a system where the results of the measurements are standardized and objective are easily conveyed to clinicians and others and will provide them with an understanding of a chronology of the effects of small treatment doses of one or more chemopreventive agents on precancerous tissue (Column 2, lines 62-67)". An ordinary practitioner would have been motivated to substitute and combine the step of administering an inducer to the test subject prior to or concomitant with observing the biomarker of Bacus et al. in the claims 48-57 of U.S. Patent No. 6,268,142 B, in order to achieve the express advantages, as noted by Bacus et al., of an invention that provides a system where the results of the measurements are standardized and objective are easily conveyed to clinicians and others and will provide them with an understanding of a chronology of the effects of small treatment doses of one or more chemopreventive agents on precancerous tissue.

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

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provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

***Claim Rejections - 35 USC § 103***

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1-7, and 16-23, and 27 are rejected under 35 U.S.C. 103(a) as being obvious over Duff et al. (U.S. Patent No. 6,268,142 B1 (July 31, 2001) in view of Bacus et al. (U.S. Patent 6,031,930) (February 29, 2000).

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Duff et al. teaches method for identifying a substance that is likely to prevent or diminish a specific biological response in a subject having an inflammatory disease-associated genotype (Example 5), the method comprising the steps of:

- a) genotyping at least one subject to identify a test subject, wherein the test subject is a subject having an inflammatory disease-associated genotype (Example 1);
- b) observing in cells obtained from the test subject, or cells propagated therefrom, at least one biomarker (IL-1 protein bioreactivity in this case) (Examples 2 and 3);
- c) contacting the cells obtained from the test subject, or cells propagated therefrom, with a test substance (Column 29, lines 43-60);
- d) observing again in the cells obtained from the test subject, or cells propagated therefrom, the at least one biomarker (Column 29, line 61 to Column 30, line 36);

wherein a change in the at least one biomarker from an inflammatory disease-associated phenotype to a non-inflammatory disease-associated phenotype identifies a test substance that is likely to prevent or diminish the specific immune response in a subject having the inflammatory disease-associated phenotype (Column 29, line 43 to Column 30, line 36 and claim 48).

Duff et al. also disclose the chromosomal region IL-1RN, and allele 1 of IL-1A(+4845), and biomarker selected from IL-1alpha production (claims 48-57).

Duff et al. also teaches inflammatory disease-associated allele from the IL-1 44112332 haplotype (Examples 4, 5, 7, and 8).

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Duff et al. also teaches inflammatory disease-associated genotype is associated with a predisposition to coronary artery disease (Example 7).

Duff et al. teaches a method, wherein at least one biomarker is selected from blood or urine IL-1alpha levels (Examples 1, 4, and 5).

Duff et al. teaches a method, wherein the cells are obtained from immune cells and immortalized cell line (Column 34, line 17 to line 61).

Duff et al. teaches a method, further comprising administering an inducer to the cells, known to activate IL-1 production in monocytes or macrophages, prior to or concomitant with each step of observing the one or more biomarkers (promoter as cited by Duff can be considered as an inducer) (Column 34, lines 17-22, and Column 33, line 62 to Column 34, line 3, and Examples 3-8).

Duff et al. do not teach the step of administering an inducer to the test subject prior to or concomitant with observing the biomarker.

Bacus et al teaches the step of administering an inducer to the test subject prior to or concomitant with observing the biomarker (Column 2, lines 17-47, Figure 15, and Column 17, line 56 to Column 18, line 5).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the step of administering an inducer to the test subject prior to or concomitant with observing the biomarker of Bacus et al. in the method of Duff et al. , since Bacus et al. states “Thus there is a need for a system where the results of the

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measurements are standardized and objective are easily conveyed to clinicians and others and will provide them with an understanding of a chronology of the effects of small treatment doses of one or more chemopreventive agents on precancerous tissue (Column 2, lines 62-67)". Further motivation is provided by Duff et al as Duff et al. states, "Methods and kits for determining whether a subject has or is predisposed to developing a disease which is associated with IL-1 polymorphisms and assays for identifying therapeutics for treating and/or preventing the development of these diseases are provided (Abstract)". An ordinary practitioner would have been motivated to substitute and combine the step of administering an inducer to the test subject prior to or concomitant with observing the biomarker of Bacus et al. in the method of Duff et al. in order to achieve the express advantages, as noted by Bacus et al., of an invention that provides a system where the results of the measurements are standardized and objective are easily conveyed to clinicians and others and will provide them with an understanding of a chronology of the effects of small treatment doses of one or more chemopreventive agents on precancerous tissue.

6. Claims 9-10 are rejected under 35 U.S.C. 103(a) over Duff et al. (U.S. Patent No. 6,268,142 B1 (July 31, 2001) in view of Bacus et al. (U.S. Patent 6,031,930) (February 29, 2000) further in view of Girtten et al. (U.S. Patent 5,760,001) (June 2, 1998).

Duff et al in view of Bacus et al. teaches the method of claims 1-7, and 16-23, and 27 as described above.

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Duff et al in view of Bacus et al. does not teach a method, wherein the inducer comprises exercise sufficient to cause exercise induced stress.

Girten et al. teach a method, wherein the inducer comprises exercise sufficient to cause exercise induced stress (Column 7, lines 20 to 53).

Duff et al in view of Bacus et al. does not teach a method, wherein the exercise is a treadmill stress test.

Girten et al. teach a method, wherein the exercise is a treadmill stress test (Example XIII, Column 18, lines 33-45).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine a method, wherein the inducer comprises exercise sufficient to cause exercise induced stress of Girten et al. in the method of Duff et al in view of Bacus et al., since Girten et al. states “Thus the present invention provides a method of restraining pathologically elevated cytokine activity in a subject (Abstract, lines 7-9)”. Further motivation is provided by Duff et al as Duff et al. states, “Methods and kits for determining whether a subject has or is predisposed to developing a disease which is associated with IL-1 polymorphisms and assays for identifying therapeutics for treating and/or preventing the development of these diseases are provided (Abstract)”. An ordinary practitioner would have been motivated to substitute and combine a method, wherein the inducer comprises exercise sufficient to cause exercise induced stress of Girten et al. in the method of Duff et al. in order to achieve the express advantages, as noted by Girten et al., of an invention that provides a method of restraining

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pathologically elevated cytokine activity in a subject, and also to achieve the express advantages, as noted by Duff et al. in view of Bacus et al., of an invention which provide methods and kits for determining whether a subject has or is predisposed to developing a disease which is associated with IL-1 polymorphisms and assays for identifying therapeutics for treating and/or preventing the development of these diseases.

7. Claims 11-15 are rejected under 35 U.S.C. 103(a) over Duff et al. (U.S. Patent No. 6,268,142 B1 (July 31, 2001) in view of Bacus et al. (U.S. Patent 6,031,930) (February 29, 2000) further in view of Hallahan et al. (U.S. Patent 5,962,424) (October 5, 1999).

Duff et al in view of Bacus et al. teaches the method of claims 1-7, and 16-23, and 27 as described above.

Duff et al in view of Bacus et al. does not teach a method, wherein the inducer comprises a subcutaneous injection of an irritant monosodium urate crystals.

Hallahan et al. teach a method, wherein the inducer comprises a subcutaneous injection of an irritant monosodium urate crystals (Example XVII, Column 43, line 64 to column 44, line 12, and Example XVI, Column 40, lines 58-63).

Duff et al in view of Bacus et al. does not teach a method, wherein the at least one biomarker includes the dimensions and/or duration of skin erythema resulting from the subcutaneous injection.

Hallahan et al. teach a method, wherein the at least one biomarker includes the dimensions and/or duration of skin erythema resulting from the subcutaneous injection. (Example XVII).

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It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine a method, wherein the inducer comprises a subcutaneous injection of an irritant monosodium urate crystals of Hallahan et al. in the method of Duff et al in view of Bacus et al., since Hallahan et al. states “The compositions and methods described are suitable for use in the delivery of selected agents to tumor vasculature, as may be used in the diagnosis and therapy of solid tumors (Abstract, last sentence)”. Further motivation is provided by Duff et al as Duff et al. states, “Methods and kits for determining whether a subject has or is predisposed to developing a disease which is associated with IL-1 polymorphisms and assays for identifying therapeutics for treating and/or preventing the development of these diseases are provided (Abstract)”. An ordinary practitioner would have been motivated to substitute and combine a method, wherein the inducer comprises a subcutaneous injection of an irritant monosodium urate crystals of Hallahan et al. in the method of Duff et al in view of Bacus et al. , in order to achieve the express advantages, as noted by Hallahan et al., of an invention that provides compositions and methods suitable for use in the delivery of selected agents to tumor vasculature, as may be used in the diagnosis and therapy of solid tumors and also to achieve the express advantages, as noted by Duff et al. in view of Bacus et al., of an invention which provide methods and kits for determining whether a subject has or is predisposed to developing a disease which is associated with IL-1 polymorphisms and assays for identifying therapeutics for treating and/or preventing the development of these diseases.

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***Response to Amendment***

8. In response to amendment, previous double patenting, 102(e), and 103(a) rejections are hereby withdrawn. However, new double patenting and 103(a) rejections are hereby included.

***Response to Arguments***

9. Applicant's arguments with respect to all pending claims have been considered but are moot in view of the new ground(s) of rejection.

***Conclusion***

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph. D., whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119. The fax phone number for this Group is (703)746-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group analyst Chantae Dessau whose telephone number is (703) 605-1237.

Arun Chakrabarti,  
Patent Examiner,

October 8, 2003

  
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**PATENT EXAMINER**

  
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